



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,940	07/12/2006	Braj Lohray	GRT/4062-190	5252

23117 7590 06/04/2010
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER

CHANG, CELIA C

ART UNIT	PAPER NUMBER
----------	--------------

1625

MAIL DATE	DELIVERY MODE
-----------	---------------

06/04/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/577,940	Applicant(s) LOHRAY, BRAJ	
	Examiner Celia Chang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Amendment and response filed by applicants dated Mar. 11, 2010 have been entered and considered carefully.

Claims 1-9, 22-24 have been canceled. Claims 10-21 are pending.

2. The rejection of claims 10-21 under 35 USC 112 second paragraph for lacking particularity and specifically pointing out applicants invention is maintained for reason of record and further rejected as new matter.

Please note that there is no antecedent basis that any of the form I being made by the process is a product having a melting point of $184\pm 3^{\circ}\text{C}$. The reference of the recited melting point was disclosed to be the form I made by the process of US 4,847,265. As it was clearly delineated in the previous office action, the Mukarram WO 2005/012300 reference provided "evidence" that pure form I of (+)-(S)-clopidogrel bisulfate has a m.p. of $198-200^{\circ}\text{C}$ and the lower m.p. products of previous literature contain "lesser" purity, i.e. mixture of other product with form I of (+)-(S)-clopidogrel bisulfate.

Because, the form I of (+)-(S)-clopidogrel bisulfate of the instant application did not name the product with any melting point, the insertion of "form I of (+)-(S)-clopidogrel bisulfate which has a melting point of $184\pm 3^{\circ}\text{C}$ " is NEW MATTER.

However, the rejection is further maintained for claim 20 for the term "such as". A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481

Art Unit: 1625

(Bd. App. 1949). In the present instance, claim 20 recites the broad recitation "linear or branched primary, secondary or tertiary alcohols", and the claim also recites "such as hexanol, 2-hexanol, 3-hexanol, isohexanol, heptanol, 2-heptanol, 4-heptanol, octanol, iso-octanol, decanol or mixtures thereof" which is the narrower statement of the range/limitation.

3. The rejection of claims 10-18, 21 under 35 USC 112 first paragraph for lacking description of "suitable" solvents is dropped in view of the cancellation of the term. However, the rejection is maintained for the "amendments" over the term "form I of (+)-(S)-clopidogrel bisulfate which has a melting point of $184\pm 3^{\circ}\text{C}$ " since no description of melting point of the products being made by the process of the instant application being what. As it was evidenced by the state of the art that form I of (+)-(S)-clopidogrel bisulfate can have a melting point of $184\pm 3^{\circ}\text{C}$ (US 4,847,265; a melting point of 181.2°C or $198-200^{\circ}\text{C}$ depending on purity (see p.3 WO2005/012300). Absent of disclosure of any melting point of the instant application or any purity description, there is no antecedent basis that the "form I" of the instant application is corresponding to a product having melting point of $184\pm 3^{\circ}\text{C}$. A survey of all the description that produced form I clopidogrel bisulfate was made:

<u>Ex</u>	<u>start</u>	<u>solvent</u>	<u>H₂SO₄</u>	<u>Seed</u>	<u>standing/stirring</u>	<u>Washing</u>
8	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
9	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
10	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
11	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
12	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
13	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C

Art Unit: 1625

14	amor- phous	n-hexanol 25-30°C	n/a	n/a	stepwise temp 22-25°C	MeOtBu 30-35°C
15	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
16	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
17	base	n-hexanol 25-30°C	dil 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
18	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
19	base	n-heptanol +H ₂ O 15-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
20	base	n-heptanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
21	base	decanol +H ₂ O 25-30°C	conc 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
22	base	decanol 25-30°C	dil 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
23	amor- phous	me-O-tBu 25-30°C	n/a	n	stirring 24hr 25-30°C	??FormII

Please note that the instant application employed “different process” from the prior art that produced the “form I of (+)-(S)-clopidogrel bisulfate which has a melting point of $184\pm 3^{\circ}\text{C}$ ”.

The new matter rejection further extends to claims 14-19 for the process making a product of “form I of (+)-(S)-clopidogrel bisulfate which has a melting point of $184\pm 3^{\circ}\text{C}$ ”. As it was evidenced that using ethylacetate produced a “form I of (+)-(S)-clopidogrel bisulfate which has a melting point of $198\text{-}200^{\circ}\text{C}$ ” (see WO 2005/012300). No description of how such claimed process would a product as “form I of (+)-(S)-clopidogrel bisulfate which has a melting point of $184\pm 3^{\circ}\text{C}$ ”.

Art Unit: 1625

4. The rejection of claims 10-21 under 35 USC 112 first paragraph as failing to comply with the enablement requirement is maintained for reason of record.

A survey of the enabled processes of making clopidogrel form I disclosed in the application is summarized as following:

<u>Ex</u>	<u>start</u>	<u>solvent</u>	<u>H₂SO₄</u>	<u>Seed</u>	<u>standing/stirring</u>	<u>Washing</u>
8	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
9	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
10	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
11	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
12	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
13	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
14	amor- phous	n-hexanol 25-30°C	n/a	n/a	stepwise temp 22-25°C	MeOtBu 30-35°C
15	base	n-hexanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
16	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
17	base	n-hexanol 25-30°C	dil 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
18	base	n-hex/H ₂ O 25-30°C	conc 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
19	base	n-heptanol +H ₂ O 15-30°C	conc 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C

Art Unit: 1625

20	base	n-heptanol 25-30°C	dil 10-25°C	y 20-25°C	stepwise temp 22-25°C	MeOtBu 30-35°C
21	base	decanol +H ₂ O 25-30°C	conc 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
22	base	decanol 25-30°C	dil 10-25°C	n	stepwise temp 22-25°C	MeOtBu 30-35°C
23	amor- phous	me-O-tBu 25-30°C	n/a	n	stirring 24hr 25-30°C	??FormII

Please note that there were exclusively three organic solvents used, n-hexanol, n-heptanol, or decanol. Water was added in the event concentrated sulfuric acid was to be used. Seeding is optional and a stepwise holding/stirring period is required. It is further evidenced that such process of making "Form I" is very specific and any change may produce other forms such as found in example 23, form I was intended but using only the washing solvent with extended period of holding/stirring will produce "form II".

5. The currently amended claims are subject to the following new grounds of rejection:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 6,429, 210 (of record).

See col. 9, lines 52-64 wherein clopidogrel free base dissolved in acetone was added 80% sulfuric acid (dilute or conc.+water) and the crystal was formed, filtered with a m.p.=184±3°C. Thus, every element of the claims have been anticipated.

Art Unit: 1625

6. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Jun. 1, 2010

/Celia Chang/
Primary Examiner
Art Unit 1625